

DESIGN OF CDR-GRAFTED ANT-*RSV* F PROTEIN VH

THE

DESIGN OF CDR-GRAFTED ANTI-RSV F PROTEIN VL

Figure 2

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly Asp Arg Val Thr	5	10	15	20	- Human KD02 VL
Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly Asp Arg Val Thr					- "CDR Grafted" VL
Asp Ile Lys Met Thr Gln Ser Pro Ser Ser Met Tyr Val Ser Leu Gly Glu Arg Val Thr					- Martine 1308F VL
Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp Leu Ala Trp Tyr Gln Gln Lys Pro	25	30	35	40	
Ile Thr Cys <u>Lys Ala Ser Gln Asp Ile Asn Arg Tyr Leu Asn</u> Trp Tyr Gln Gln Lys Pro					
Ile Thr Cys Lys Ala Ser Gln Asp Ile Asn Arg Tyr Leu Asn Trp Phe Gln Gln Lys Pro					
		CDR 1			
Gly Lys Ala Pro Lys Leu Leu Ile Tyr <u>Arg Ala Asn Arg Leu Val Asp</u> Gly Val Pro Ser	45	50	55	60	
Gly Lys Ser Pro Lys Thr Leu Ile His Arg Ala Asn Arg Leu Val Asp Gly Val Pro Ser					
		CDR 2			
Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro	65	70	75	80	
Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro					
Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Phe					
Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Ser - - -	85	90	95	100	
Asp Asp Phe Ala Thr Tyr Tyr Cys <u>Leu Gln Phe His Glu Phe Pro Tyr Thr</u> Phe Gly Gly					
Glu Asp Met Gly Ile Tyr Tyr Cys Leu Gln Phe His Glu Phe Pro Tyr Thr Phe Gly Gly					
		CDR 3			
		<<V / >>>			
- - - - -	105				
Gly Thr Lys Leu Glu Ile Lys					
Gly Thr Lys Leu Glu Ile Lys					

cgcggatccatggacatgaggtgccg
 MetAspMetArgValProAlaGlnLeuLeuGlyLeuLeuLeuLeuTrpLeuProGlyAla
 1 ~~caatgacatgaggtgccgctcagctcctgggactcttgcctgacatgggctcctcaggtgcc~~
 TACCTGTACTCCCAGGGGCGAGTCGAGGACCCCGAGGACGACGAGACCGAGGGTCCACGG

 LysCysAspIleGlnMetThrGlnSerProSerThrLeuSerAlaSerValGlyAspArg
 61 ~~aaatgacatgaggtgccgctcagctcctgggactcttgcctgacatgggctcctcaggtgcc~~
 TTACACTATAGGTCTACTGGGTCAGAGGAAGGTGGGACAGACGATGACATCCTCTGTCT

 ValThrIleThrCysLysAlaSerGlnAspIleAsnArgTyrLeuAsnTrpTyrGlnGln
 121 ~~gtcaccatcacttgcaaggcgagtcaggacattaataggtattttaactggtagcagcag~~
 CAGTGGTAGTGAACGTTCCGCTCAGGCCGTAAATTATCCATAAATTGACCATGGTCTCT

 LysProGlyLysAlaProLysLeuLeuIleTyrArgAlaAsnArgLeuValAspGlyVal
 181 ~~aaacccgggaagccoctagatgacatgaggtgccgctcagctcctgggactcttgcctgacatgggctcctcaggtgcc~~
 TTGAGGCTTTTCGGGGATTTCGAGGACTAGATAGCACGTTTGTCTAACCATCTACCCAG

 ProSerArgPheSerGlySerGlyThrGluPheThrLeuThrIleSerSerLeu
 241 ~~ccatcaggttcagccgacgtcagctcctgggactcttgcctgacatgggctcctcaggtgcc~~
 GGTAGTTCGAAGTCGCCGTCACCTAGACCCTTCTCTTAAGTGAGAGTGGTAGTCTGGGAG

 GlnProAspAspPheAlaThrTyrTyrCysLeuGlnPheHisGluPheProTyrThrPhe
 301 ~~cagcctgatgattttgcaacttattactgcctacagtttcattgagtttccgtacacgttc~~
 GTGGGACTACTAAAACGTTGAATAATGACGGGATGTCAAAGTACTCAAAGGCATGTGCAAG
 3' gtgcaag

 GlyGlyGlyThrLysLeuGluIleLys
 361 GGAGGGGGGACCAAGCTTGAATAAAA 3'
 CCTGGGGGGGCTGGTTCGAACCTTTATTTT 5'
 cctccccctggttcgaaccc 5'

Figure 4. Oligos used to make H2308 VL

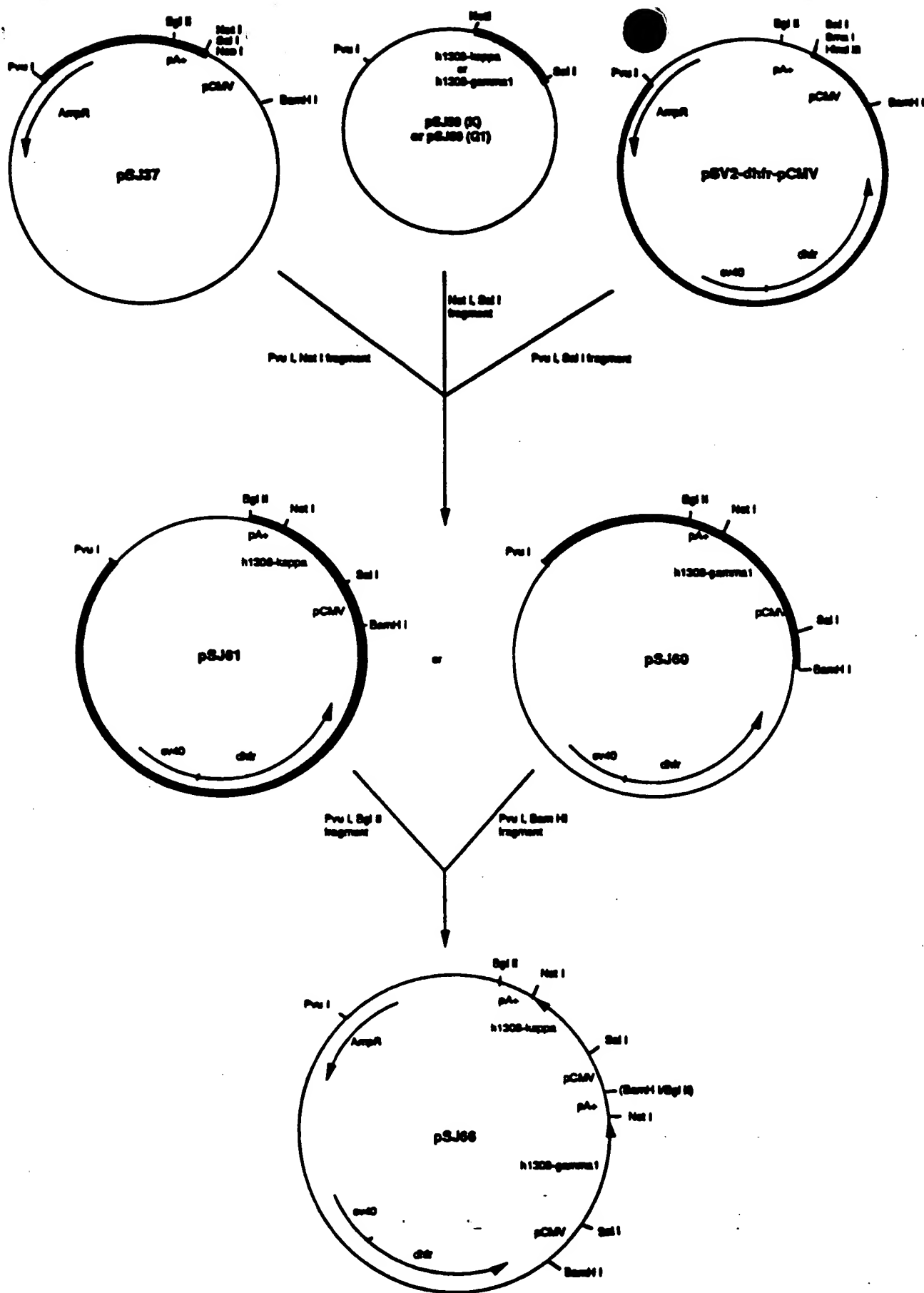


Fig 5. Construction of the Humanized 1308 expression vectors

Neutralization of RSV

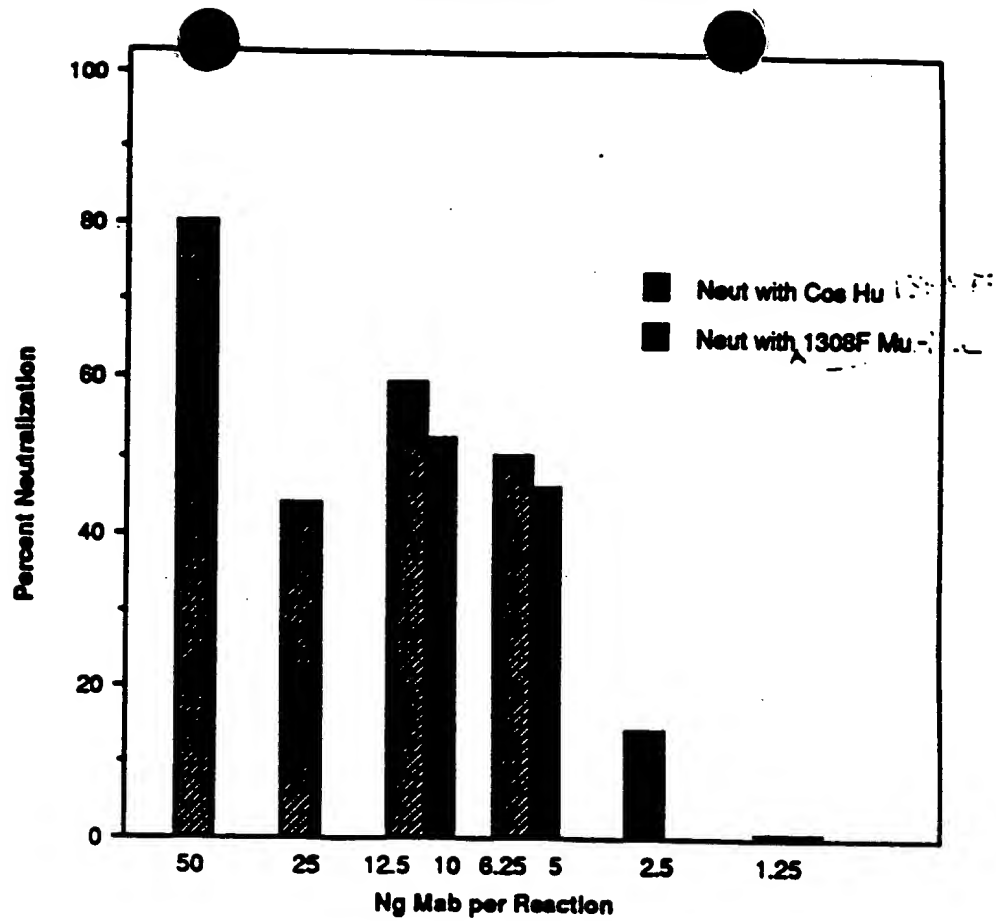


FIGURE 6

86T260-02F85F60

Design of Humanized VH f r anti-RSV Mab 1129

5 10 15
 Gln Val Thr Leu Arg Glu Ser Gly Pro Ala Leu Val Lys Pro Ser Human VH (Cor)
 1 Gln Val Thr Leu Arg Glu Ser Gly Pro Ala Leu Val Lys Pro (Ser) "Humanized" VH
 Gln Val Glu Leu Gln Glu Ser Gly Pro Gly Ile Leu Gln Pro Ser Murine 1129 VH

 Gln Thr Leu Thr Leu Thr Cys Ser Phe Ser Gly Phe Ser Leu Ser
 16 Gln Thr Leu Thr Leu Thr Cys Ser Phe Ser Gly Phe Ser Leu Ser
 Gln Thr Leu Ser Leu Thr Cys Ser Phe Ser Gly Phe Ser Leu Ser

 Ser Ser Gly Met Cys Val Gly Trp Ile Arg Gln Pro Pro Gly Lys
 31 Thr Ser Gly Met Ser Val Gly Trp Ile Arg Gln Pro Pro Gly Lys
 Thr Ser Gly Met Ser Val Gly Trp Ile Arg Gln Pro Ser Gly Glu

 Ala Leu Glu Trp Leu Ala Asp Ile Glu Trp Asp Asp Asp Lys Asp
 46 Ala Leu Glu Trp Leu Ala Asp Ile Trp Trp Asp Asp Lys Lys Asp
 Gly Leu Glu Trp Leu Ala Asp Ile Trp Trp Asp Asp Lys Lys Asp

 Tyr Asn Thr Ser Leu Asp Thr Arg Leu Thr Ile Ser Lys Asp Thr
 61 Tyr Asn Pro Ser Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr
 Tyr Asn Pro Ser Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr

 Ser Lys Asn Gln Val Val Leu Thr Val Thr Asn Val Asp Pro Ala
 76 Ser Lys Asn Gln Val Val Leu Lys Val Thr Asn (Val) Asp Pro Ala
 Ser Ser Asn Gln Val Phe Leu Lys Ile Thr Gly Val Asp Thr Ala

 Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Ile Thr Val Ile Pro Ala Pro Ala Gly
 91 Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Ser Met Ile Thr Asn Trp - - -
 Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Ser Met Ile Thr Asn Trp - - -

 Tyr Met Asp Val Trp Gly Arg Gly Thr Pro Val Thr Val Ser Ser
 106 Tyr Phe Asp Val Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser
 Tyr Phe Asp Val Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser

Figure 7

09158120-092198

DESIGN OF CDR-~~GRAFTED~~ ANTI-RSV MAb 1129 VL

5 10 15
 Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val - Human K102 VL
 Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val - "CDR Grafted" VL
 Asp Ile Gln Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro - Murine 1129 VL

20 25 30
 Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser
 Gly Asp Arg Val Thr Ile Thr Cys Lys Cys Gln Leu Ser Val Gly
 Gly Glu Lys Val Thr Met Thr Cys Ser Ala Ser Ser Ser Val Gly CDR 1

35 40 45
 Ser Trp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys
Tyr Met His - Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys
 Tyr Met His - Trp Tyr Gln Gln Lys Ser Ser Thr Ser Pro Lys

50 55 60
 Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu Ser Gly Val Pro Ser
 Leu Trp Ile Tyr Asp Thr Ser Lys Leu Ala Ser Gly Val Pro Ser
 Leu Trp Ile Tyr Asp Thr Ser Lys Leu Ala Ser Gly Val Pro Gly CDR 2

65 70 75
 Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile
 Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile
 Arg Phe Ser Gly Ser Gly Ser Gly Asn Ser Tyr Ser Leu Thr Ile

80 85 90
 Ser Ser Leu Gln Pro Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln
 Ser Ser Leu Gln Pro Asp Asp Phe Ala Thr Tyr Tyr Cys Phe Gln
 Ser Ser Ile Gln Ala Glu Asp Val Ala Thr Tyr Tyr Cys Phe Gln

95 100 105
 Tyr Asn Ser Tyr Ser
Gly Ser Gly Tyr Pro Phe Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
 CDR 3
Gly Ser Gly Tyr Pro Phe Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys

<<V / J>>

Figure 8

09158120-092198

SECRET

Figure 9

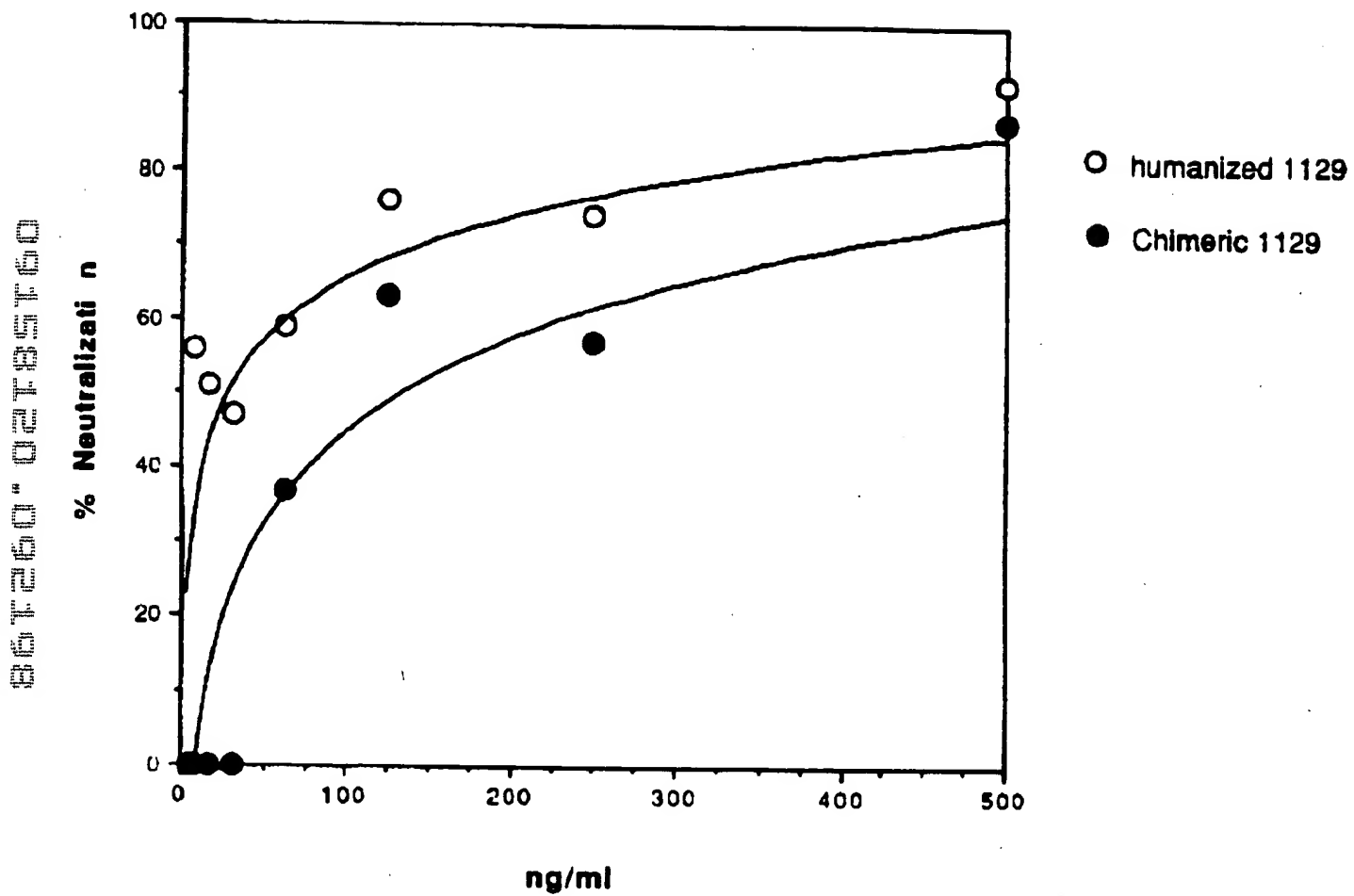


Figure 10